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DIAGNOSIS OF ORTHOSTATIC HYPOTONICITY

O. Thulesius and U. Ferner

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16. Abstract

The author investigates relationships between blood pressure and heart rate on the one hand, and age, weight and height on the other. On this basis he derives norms for the general diagnosis of circulatory disturbances.

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DIAGNOSIS OF ORTHOSTATIC HYPOTONICITY

O. Thulesius and U. Ferner[1]

A hypotonic arterial circulation difficulty is present only if under certain situations of stress, i.e., in changing position or in standing, symptoms of reduced organ transfusion, e.g., on the part of the brain, occur. Low blood pressure by itself, let us say under 110 mm Hg for adults, is in no wise a proof for a hypotonic circulatory disturbance, although such a disturbance may occur in patients with untreated hypertonicity [21]. In addition the exhaustive hemodynamic studies of Frick [7] have unambiguously shown that circulatory regulation in asymptomatic hypotonic patients is clinically normal. Naturally a hypotonic disturbance in regulation will show up more often in cases with a low blood pressure, because here every drop in blood pressure leads closer to the critical limit of cerebral ischemia. /742*

Therefore it is necessary to obtain a more precise conclusion about the nature of a possible circulatory disturbance in defining hypotonic circulatory disturbances with the assistance of purposeful anamnesis and through objective orthostatic tests. This is possible with tilting table process, a squatting test, or simply with a standing test. In clinical practice it is desirable to carry out the examination as simply as possible according to certain standardized norms. The purpose of this work was to work out "normal values" for the standing test.

Material and Method

The reaction of heart rate frequency and blood pressure on a change in body position was recorded for 86 healthy subjects of both sexes. Classification of the subjects with data about average age, size and weight can be seen from Table 1. Normal anamnesis, chest x-ray, EKG examination, blood pressure measurement and elimination of any medicines were required to exclude any pathological cases.

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[1]Medical Research Division, Sandoz AG, Basel.
*Numbers in the margin indicate foreign pagination.

TABLE 1. MEAN VALUES ($\bar{x}$) AND STANDARD DEVIATIONS (s) OF THE "AGE, WEIGHT, SIZE" PARAMETERS

	Age in Years		Weight in kg		Size in cm	
	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	s
Total Group N = 86	38.92	± 12.39	67.21	± 10.17	170.00	± 9.14
Male Subjects N = 40	36.78	± 13.84	70.62	± 11.18	174.60	± 9.72
Female Subjects N = 46	41.26	± 10.83	64.24	± 8.22	166.00	± 6.40
Subjects 20-29 Years Old N = 20	22.85	± 3.08	67.00	± 8.84	175.20	± 9.12
Subjects 30-39 Years Old N = 27	34.37	± 2.83	64.52	± 9.38	170.00	± 8.59
Subjects 40-49 Years Old N = 14	43.86	± 3.13	63.50	± 6.25	164.90	± 5.36
Subjects 50-63 Years Old N = 25	54.80	± 3.49	72.36	± 12.00	168.80	± 9.76

Heart rate and blood pressure were measured in a lying position after 5 and 10 minutes, immediately after standing up, and finally 7 minutes after standing. Heart rate was determined continuously from EKG curves and blood pressure was measured by ausculation according to Riva Rocci with a cuff 12 cm wide and 32 cm long on the upper arm.

The measurement values of the previous studies were statistically evaluated, particularly in reference to average values and variability of heart rate and blood pressure in a lying position and at each point of time while standing. In addition the differences between lying and standing were investigated in order to establish normal values. Finally a check was made to see to what extent such factors as sex, age, weight and height influence measurement values. The arithmetical means, the standard deviations and the coefficients of variability were computed for the statistical analysis. A check was made at the same time to see whether measurement magnitudes follow a normal distribution [8]. Normality was assumed for a more precise statistical analysis. The likewise tabulated higher moments of distribution, the slope and excess, provide, in the case of possible deviation from normality, an inference about whether the distribution of measured values is unsymmetrical, i.e., biased left or right, too flat or too high. The measurement magnitudes proved predominantly to be distributed normally.

Results

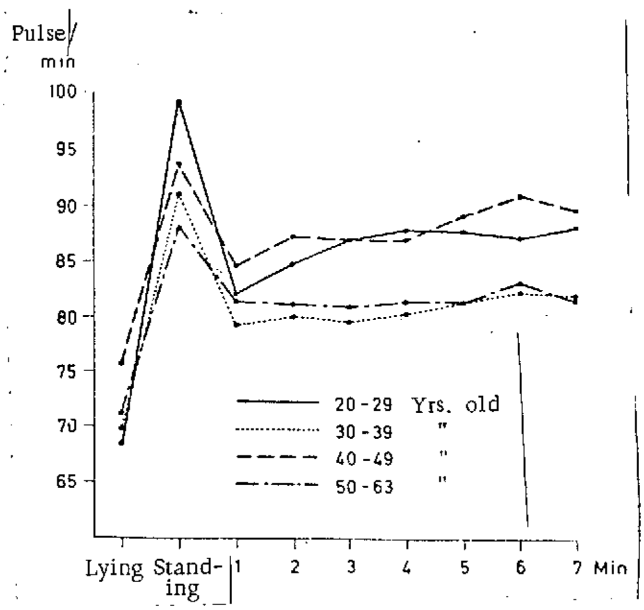

Figure 1. Profiles of Pulse Frequency Lying, After Standing Up, and During 7 Minutes of Standing.

Heart Rate. In lying the heart rate was constant after 5 and 10 minutes (i.e., no significant difference in measured values between the two points of time). The total course of heart rate when standing was on the average 20% higher than in lying. Immediately after standing up (about 10 seconds after changing position) a considerable rise in heart rate occurred, 31% in the total group in comparison with the value when lying. After one minute the heart rate slowed again and in the further course of the test stabilization took place. The profiles of pulse frequence are presented in Figure 1 and the measured values of the entire group in Table 2.

TABLE 2. HEART RATE (TOTAL GROUP - N = 86)

	Mean value	Standard deviation	Coefficient of Variability	Slope	Excess	Deviation from normality
Lying (10 min.)	70.71	± 11.60	16.41	0.411	2.756	n.s.
Standing up	92.38	± 15.62	16.91	0.113	2.693	n.s.
After 1 minute	81.23	± 13.27	16.34	0.486	3.100	*
After 2 minutes	82.67	± 12.64	15.29	0.282	2.814	n.s.
After 3 minutes	83.07	± 12.38	14.90	0.371	3.157	*
After 4 minutes	83.55	± 12.63	15.12	0.356	2.959	n.s.
After 5 minutes	84.40	± 13.08	15.50	0.396	3.095	n.s.
After 6 minutes	85.20	± 13.06	15.33	0.658	3.204	*
After 7 minutes	85.30	± 13.60	15.94	0.551	3.085	n.s.

n.s. = not significant (probability of error $P > 0.05$).
* = slightly significant (probability of error $P \leqslant 0.05$).

Blood Pressure. During the standing test systolic blood pressure did not indicate any very large changes. The percentage deviation, with a slight drop of under 1% during the test, is statistically invisible. On the other hand, the diastolic blood pressure showed a significant increase, by 11% after 7 minutes of standing. This also indicates a reduction in blood pressure amplitude by about 18%. The progress of blood pressure reaction is graphically presented in Figure 2, and the measurements are found in Tables 3, 4, 5 and 6.

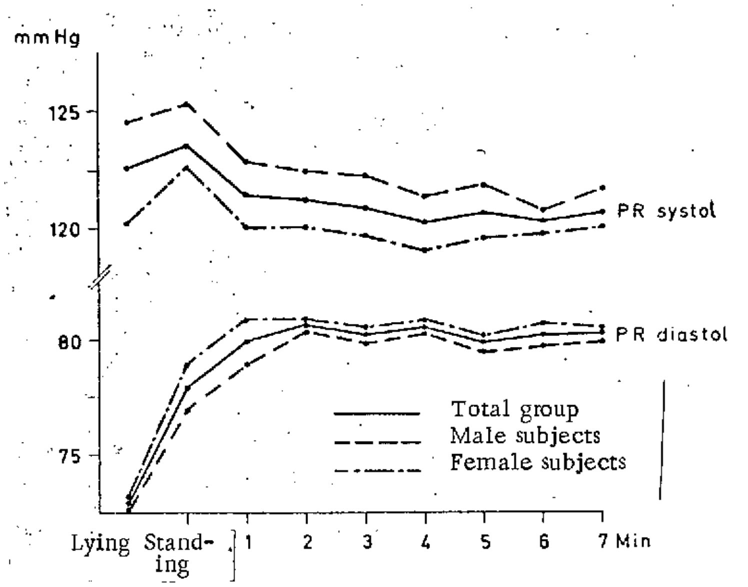

Figure 2. Profiles of Systolic and Diastolic Blood Pressure Lying Down, After Standing Up and During 7 Minutes of Standing.

TABLE 3. SYSTOLIC BLOOD PRESSURE (mm Hg) (TOTAL GROUP - N = 86)

	Mean value	Standard deviation	Coefficient of Variability	Slope	Excess	Deviation from normality
Lying (10 min.)	122.4	± 13.03	10.65	0.452	2.351	n.s.
Standing up	123.9	± 14.07	11.36	0.364	2.709	n.s.
After 1 minute	121.5	± 13.24	10.89	0.343	2.756	n.s.
After 2 minutes	121.3	± 11.89	9.90	0.365	2.707	n.s.
After 3 minutes	121.0	± 12.10	10.00	0.238	2.315	n.s.
After 4 minutes	120.4	± 11.81	9.81	0.344	2.842	n.s.
After 5 minutes	120.9	± 12.87	10.65	0.313	2.808	n.s.
After 6 minutes	120.6	± 12.61	10.46	0.399	2.578	n.s.
After 7 minutes	121.2	± 12.12	10.00	0.399	2.469	n.s.

n.s. = not significant (probability of error P > 0.05).

TABLE 4. DIASTOLIC BLOOD PRESSURE (mm Hg) (TOTAL GROUP - N = 86).

	Mean value	Standard deviation	Coefficient of Variability	Slope	Excess	Deviation from normality
Lying (10 min.)	72.97	± 9.71	13.31	0.294	2.808	n.s.
Standing up	78.20	± 9.30	11.89	0.071	2.688	n.s.
After 1 minute	80.06	± 9.50	11.87	0.128	2.466	n.s.
After 2 minutes	80.81	± 9.64	11.93	0.105	2.286	n.s.
After 3 minutes	80.41	± 9.02	11.22	0.023	2.968	n.s.
After 4 minutes	80.70	± 8.95	11.09	0.346	3.108	*
After 5 minutes	80.17	± 8.28	10.33	0.195	2.860	n.s.
After 6 minutes	80.58	± 8.52	10.57	0.349	3.393	*
After 7 minutes	80.58	± 8.52	10.57	0.349	3.427	*

n.s. = not significant (probability of error $P > 0.05$).
* = slightly significant (probability of error $P \leqslant 0.05$).

TABLE 5. MEAN VALUES OF BLOOD PRESSURE AMPLITUDE (mm Hg)

	Total group	Male Subjects	Female Subjects	20-29 Years old	30-39	40-49	50-63
Lying (10 minutes)	49.5	51.5	47.6	48.7	49.7	46.8	51.2
Standing up	45.7	48.0	43.7	45.3	47.6	44.0	45.0
After 1 minutes	41.5	44.1	39.2	35.7	44.3	40.4	43.6
After 2 minutes	40.5	42.1	39.2	35.3	41.7	37.9	45.0
After 3 minutes	40.6	42.3	39.2	34.0	42.5	38.6	45.0
After 4 minutes	39.7	41.2	38.4	33.2	41.7	37.6	44.0
After 5 minutes	40.8	42.3	39.5	33.0	42.9	39.3	45.6
After 6 minutes	40.1	41.1	39.1	32.0	42.1	38.6	45.0
After 7 minutes	40.7	41.7	39.7	32.8	42.5	38.9	45.8

Correlation. It should be made clear whether correlations for the differences at the initial value occur for heart rate and blood pressure (i.e., whether the standing values are correlated with the resting values). Here it can be established that this is not true of heart rate. It is true of systolic blood pressure that statistically significant to highly significant correlations exist between the differences of systolic blood pressure from the resting position to standing and the initial value, both after one minute and after seven minutes after standing up; i.e., the greater the initial value of the systolic blood pressure, the greater its decline when standing ($P < 0.05$-0.001). /746
It is to be established for diastolic blood pressure that statistically highly

significant correlations exist between the differences of diastolic blood pressure in the resting position in the initial values, both after one minute and seven minutes after standing up ($P < 0.001$), i.e., it is also true here that the higher the initial value of the diastolic blood pressure, the greater is its modification when standing. It is also true that there is no significant dependence between the differences in heart rate when resting and body weight. However, there is a significant dependence between the differences in systolic blood pressure in the resting position and the weight of the subjects, after both one minute and after seven minutes, i.e., the higher the weight, the greater the decline in values when lying ($P < 0.05$). Between the differences of heart rate at rest and height there is a significant dependence after both /748 one and seven minutes ($P < 0.05$), i.e., the taller the subjects are, the more the heart rate increases when standing. Finally, we were able to determine that a significant relationship exists between the differences in systolic blood pressure in the resting position and the height of the subjects after seven minutes and in a reduction of both differences (one and seven minutes when standing), i.e., the taller the subjects are, the greater is also the drop in the systolic blood pressure in relation to lying ($P < 0.01$). Age: basically immediate increase in heart rate after standing up is highest among the youngest individuals (44% in the 20-29 year old group and 24% in the 40-49 year old group). However, in the further conduct of the test the differences are no longer so marked (see Figure 1). After seven minutes of standing statistically certain differences exist only between the 20-29 year old group, the 30-39 year old group, and the 50-63 year old group, with the youngest age group exhibiting the greatest pulse values. Similar relationships are also true for the percentage modifications of the diastolic blood pressure (cf. Table 6). Sex: sex-specific differences were able to be identified in only a few parameters, namely for the average modifications in systolic blood pressure, which were greater in the male subjects after seven minutes of standing (cf. Table 6). For technical reasons only correlations between one co-variable and the goal-variable [Translator's note: goal-variable in German could be misspelling for time-variable] were examined. However, for deeper study in this direction it appears proper for a functional relationship among a number of influential magnitudes to be considered for magnifications in blood pressure and heart rate.

TABLE 6. PROGNOSES, DIFFERENCES COMPARED TO INITIAL (RESTING) POSITION.

	Heart rate		Systolic blood pressure		Diastolic blood pressure	
	After 1 minute	After 7 minutes	After 1 minute	After 7 minutes	After 1 minute	After 7 minutes
Total group	10.21 ± 15.56	14.26 ± 17.60	−1.11 ± 17.46	−1.28 ± 15.04	7.27 ± 15.84	7.56 ± 15.40
Male subjects	11.57 ± 15.15	15.65 ± 19.50	−2.25 ± 18.12	−3.13 ± 14.62	6.00 ± 15.95	6.63 ± 16.81
Female subjects	9.02 ± 16.24	13.04 ± 16.30	−0.11 ± 17 46	0.33 ± 15.35	8.37 ± 16.16	8.37 ± 16.48
Subjects 20-29 years old	12.75 ± 17.10	19.15 ± 21.61	−1.00 ± 16.14	−2.75 ± 12.75	12.75 ± 20.67	13.25 ± 16.76
Subjects 30-39 years old	8.44 ± 16.09	12.93 ± 15.32	−0.19 ± 20.10	−0.03 ± 12.31	5.37 ± 14.46	6.11 ± 14.59
Subjects 40-49 years old	8.93 ± 21.21	14.50 ± 21.35	−0.36 ± 20.83	−2.50 ± 19.53	6.79 ± 16.20	5.71 ± 15.12
Subjects 50-63 years old	10.80 ± 13.42	11.64 ± 15.81	−3.00 ± 17.68	0.20 ± 19.76	5.20 ± 12.31	5.60 ± 14.64

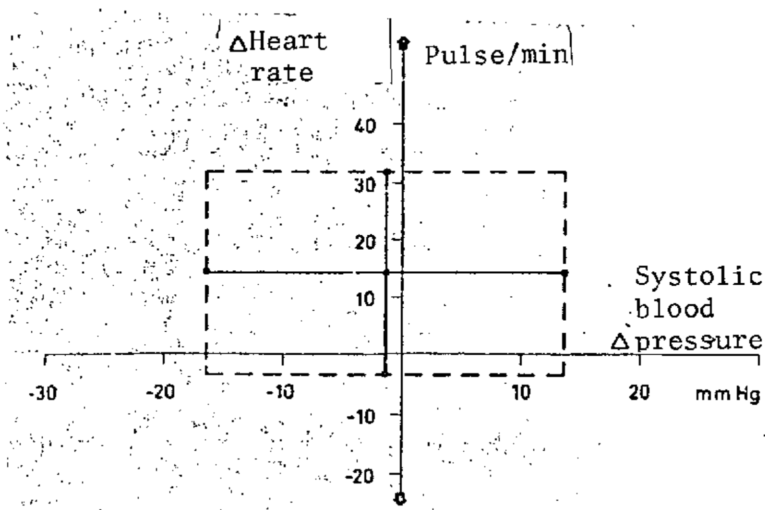

Figure 3. Prognosis Intervals, i.e., Variation in Blood Pressure and Pulse When Standing with ±2 Standard Deviations from the Mean.

Calculation of Prognosis Intervals. We calculated the arithmetical means and the standard deviations with the help of our measured values. On the basis of these parameters intervals are to be set up containing independent, future "normal values" with an assumed certainty, let us say of 95%. We had defined the calculated intervals as prognosis intervals. They ought to be put to use in a purely practical way for the diagnosis of pathological cases with orthostatic dysregulation. Intervals of this type are found with normally distributed observations. Barring a few exceptions, this presumption of normality is accepted. The calculated prognosis intervals or normal ranges for heart rate, systolic blood pressure and diastolic blood pressure can be seen in Table 6 for all groups and for each control. Figure 3 gives a graphic representation for the entire group after 7 minutes of standing.

Evaluation of the Orthostatic Test

We have earlier reported on a diagram for easy evaluation of circulatory magnitudes when standing [22]. This has the advantage of providing a rapid inference about the different physiological and pathological reaction types, and can therefore be applied for diagnostic purposes and for evaluation of treatment results. In order to make the evaluation, the deviations in systolic blood pressure and heart rate are introduced into a coordinate system, such as can be seen in Figure 4. The intersection of the x and y axes, thus the zero point for the coordinate system, represents the initial value when lying for both blood pressure and heart rate. The variation in blood pressure produced while standing, let us say after 7 minutes of standing, is plotted on the x axis, rising to the right and falling to the left. In the same way the modification in heart rate is plotted on the y axis, pulse increase upward and decrease downward. In this way we get points in the coordinate system which characterize the heart rate and blood pressure reaction occasioned by standing. In addition the normal ranges for orthostatic modifications in (systolic) blood pressure and heart rate are provided in the diagram. These correspond to the statistically determined prognosis intervals mentioned above. Depending on the position of the points in the coordinate system, a rapid determination can be made of whether the values fall within the normal range or not, and are or are not probable expressions of disregulation.

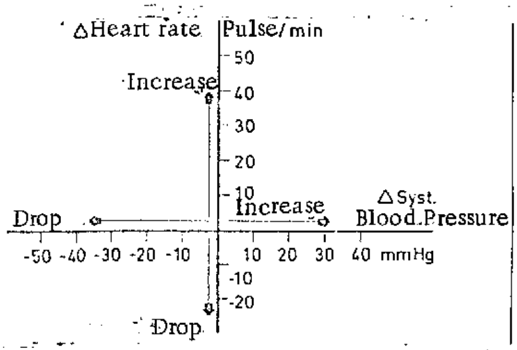

Figure 4. The Coordinate System for Plotting Orthostatic Modifications in Blood Pressure and Pulse (Δ Values) When Standing. The intersection of the blood pressure and axis and the pulse axis (zero point) is the initial value, and the modifications are plotted on the coordinate system in accord with the sign (plus or minus).

In addition to the central normal range around the zero point, four pathological "reaction types" can be basically distinguished, and this is done by using the rate-pressure diagram in the following way (see Figure 5):

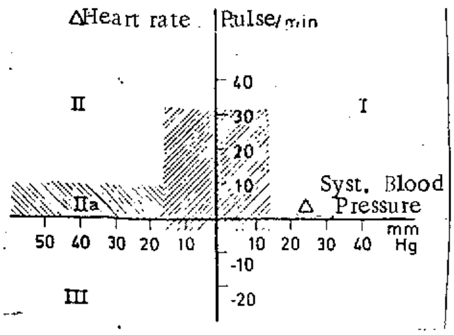

Figure 5. Classification of the Orthostatic Circulatory Difficulties According to the Frequency-Pressure Diagram. The central range, hatched toward the right, presents the normal variation. I-III designate pathological reaction types (see text).

Type I: Hypertonic reaction: rise in heart rate and blood pressure.

Type II: Sympathicotonic reaction: rise in heart rate and drop in systolic blood pressure.

Type IIa: Asympathicotonic reaction: deeper drop of both systolic and diastolic blood pressure with missing or weakened pulse reaction.

Type III: Vasovagal reaction: Drop in blood pressure with simultaneous reduction in heart rate.

This diagnostic classification corresponds to the pathopsychological grouping of Table 7. The example in Figure 6 serves to explain this principle in more detail.

TABLE 7. /751

1. Sympathicotonic Hypotension
   a) Idiopathic (genetically determined?)
   b) Oligemia (reduced blood plasma volume)
   c) Sequestration: varices (Arenander, 1960), thermodilation of skin vessels, venodilation by nitrites
   d) Pregnancy (Pyorala, 1966)
   e) Lack of conditioning: lying in bed, weight loss because of gravity elimination
   f) Post-infectious: virus infection, encephalitis, meningitis, myocarditis.

2. Asympathicotonic Hypotension
   a) Neurogenic (Goodall et al., 1968) collier idiopathic Postural Hypotension (Bradbury and Eggleston, 1925). With peripheral (Sharpey-Schafer and Taylor, 1960) and central neuropathy (Shy and Drager, 1960)
   b) Iatrogenic forms following thoraco-lumbar sympathectomy and administration of ganglion blocks (McIntosh et al., 1954).

3. Vasovagal Hypotension
   a) Acute syncope when standing (Brigden et al., 1950)
   b) Traumatic reactions, fright reaction.

4. Special Forms

   a) Vestibular myxoma.

   b) "Supine hypotensive syndrome" (Howard et al., 1953).

   c) Cardial forms, e.g., left-right-shunt (Bachmann et al., 1968).

   d) Sinus caroticus syndrome (Francke, 1968).

   e) Endocrine forms (Siegenthaler, 1970).

   f) Iatrogenicity, after administration of phenothiazine, antidepressants.

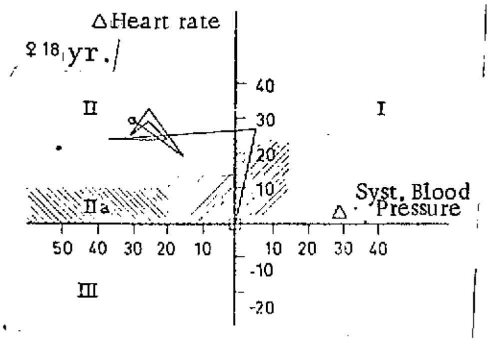

Figure 6. Example of a Pathological Reaction Ending in Quadrant II, i.e., a Case of Sympathicotonic Orthostatismus (Drop in Systolic Blood Pressure with 30 mm Hg and Pulse Increase at 30/min).

Discussion

Evaluation of circulatory adaptation when standing with the help of the systolic blood pressure and heart rate has the advantage of indicating the most important aspects of orthostatic disregulation in a majority of cases, i.e., a possible greater drop in heart volume per minute (systolic blood pressure) and the extent of reflex sympathetic compensatory activity on the part of the baroreceptors (heart rate). This type of consideration deviates from the classification of orthostatic disregulation according to Schellong [17] and Delius [5] to the extent that they first evaluate modifications in diastolic blood pressure. However, variations in diastolic blood pressure must primarily be attributed to reflex modifications in peripheral vessel resistance, and therefore this is a parameter which provides more of an inference about the amount of compensatory vasoconstriction than it does directly about the primary drop in heart volume per minute on the basis of diminished venous return. The latter is best shown to an approximate degree by the modification in blood pressure amplitude [9]. For this reason when /752
it is a matter of purely practical clinical diagnostic definition, an evaluation of the systolic blood pressure and pulse on the basis of a diagram [22] seems reasonable. The decisive point in all types of orthostatismus, as it is in normal standing reaction, is the dropping of the volume per minute, and the second point, decisive for the pathophysiological type, is the degree of sympatho-adrenalin counter-regulation, and here the heart rate seems to be the best indicator.

Naturally consistent execution of an orthostatic test, such as the evaluation suggested here, also has essential significance for rational treatment of the circulatory difficulty in question. The most frequent type of orthostatic hypotonicity by far is the sympathicotonic form, where the drop in blood pressure is accompanied by a marked rise in heart rate [22]. In this type of disturbance both the modification in heart rate, in the sense of tachycardia, and the rise in diastolic blood pressure provide an indirect inference about the extent of sympathetic counter-regulation. However, direct proofs of a rise in the neuro-humoral sympathetic activity are available, namely the investigations of Vendsalu [23], who was able to show clearly that in all cases of sympathicotonic orthostatic hypotonicity the endogenic secretion of catecholamines is sharply increased. In this regard it seems less reasonable to apply preparations which give evidence of effects similar to those of catecholamines, particularly those which have a β-receptor activating heart effect (intensification of tachycardia). It would be much better if the medical therapy were directed at the fundamental cause of the sympathicotonic hypotonia: defective venous constriction [24]. This goal can be accomplished, e.g., by using dihydroergotamine, a substance with specific venoconstrictor qualities [14].

The schematic evaluation described here for the orthostatic circulation reactions is based on the so-called Marey Law, which refers to the reciprocal relationship of heart rate and blood pressure with acute alterations in blood pressure homeostasis [12]. Correspondingly an acute drop in mean arterial pressure leads by way of the baroreceptors to a reflectional rise in heart rate, primarily by means of vagus inhibition and secondarily by a rise in sympathicotonia. In this case the rate modification is directly dependent upon the extent of the primary blood pressure change. Under these conditions, therefore, the heart rate is an indicator of the extent of orthostatic blood pressure difficulty. It is generally true that the reflectional rise in diastolic blood pressure corresponds to the change in heart rate, and is thus also an expression of predominant sympathicotonia. However, the adjustment of the heart rate in acute circulatory reversals is considerably faster (see Figure 7). In the case of sympathetic damage in the sense of a neural postural hypotension (see Table 7), there is first a drop in the compensatory resistance increase (no rise or a drop in diastolic blood pressure) as the sympathetic problem increases. Then comes a reduced or completely missing pulse compensation. In certain types of narcosis the central reflectional control of the blood pressure disappears and under such conditions we can find paradoxical reactions characterized by bradycardia during the first hydrostatically caused drop in the arterial pressure [16]. In these cases the heart centered Bainbridge Reflex (dependence of heart rate on pressure in the right vestibule) seems to dominate baroreceptor control. /753

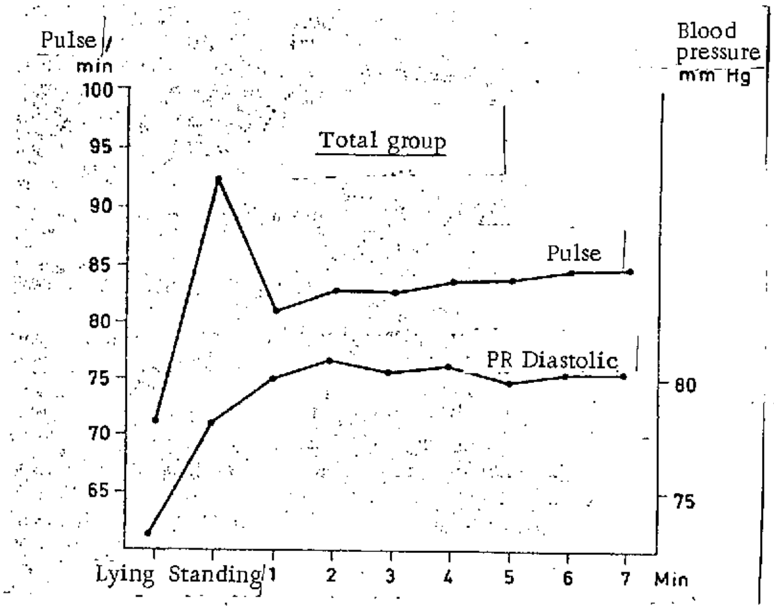

Figure 7. Reaction Shape of Heart Rate and Diastolic Blood Pressure When Lying, After Standing up, and While Standing. The more rapid reaction of the heart rate should be noted (slower rise in diastolic blood pressure when standing).

Summary

A new principle for the diagnostic evaluation of orthostatic circulatory disturbances is presented. The method is based upon a simple orthostatic test with recording of blood pressure and heart rate in the supine position and during 7 minutes' standing. In order to differentiate between normal and abnormal reactions we have compiled control data from 86 healthy individuals of both sexes with an age range of 20-63 years together with a statistical /754 analysis of the material. The normal range of heart rate and blood pressure has especially been considered after 1 and 7 minutes in the upright position, and

with the aid of a graphical analysis using a coordinate-system the diagnostic evaluation is facilitated.

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